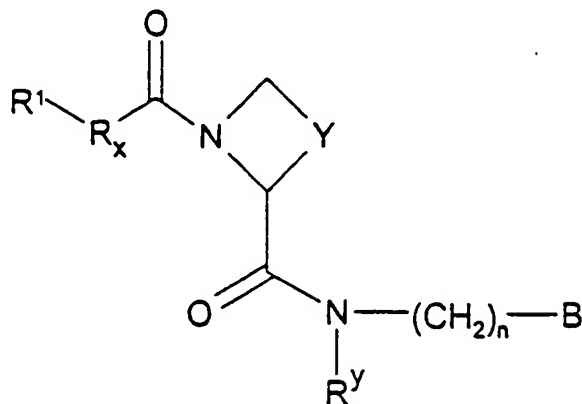


**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1 (original). A compound of formula I,



wherein

R<sup>1</sup> represents H, C<sub>1-4</sub> alkyl (optionally substituted by one or more substituents selected from cyano, halo, OH, C(O)OR<sup>1a</sup> or C(O)N(R<sup>1b</sup>)R<sup>1c</sup>) or OR<sup>1d</sup>;

R<sup>1d</sup> represents H, C(O)R<sup>11</sup>, SiR<sup>12</sup>R<sup>13</sup>R<sup>14</sup> or C<sub>1-6</sub> alkyl, which latter group is optionally substituted or terminated by one or more substituent selected from OR<sup>15</sup> or (CH<sub>2</sub>)<sub>q</sub>R<sup>16</sup>;

R<sup>12</sup>, R<sup>13</sup> and R<sup>14</sup> independently represent H, phenyl or C<sub>1-6</sub> alkyl;

R<sup>16</sup> represents C<sub>1-4</sub> alkyl, phenyl, OH, C(O)OR<sup>17</sup> or C(O)N(H)R<sup>18</sup>;

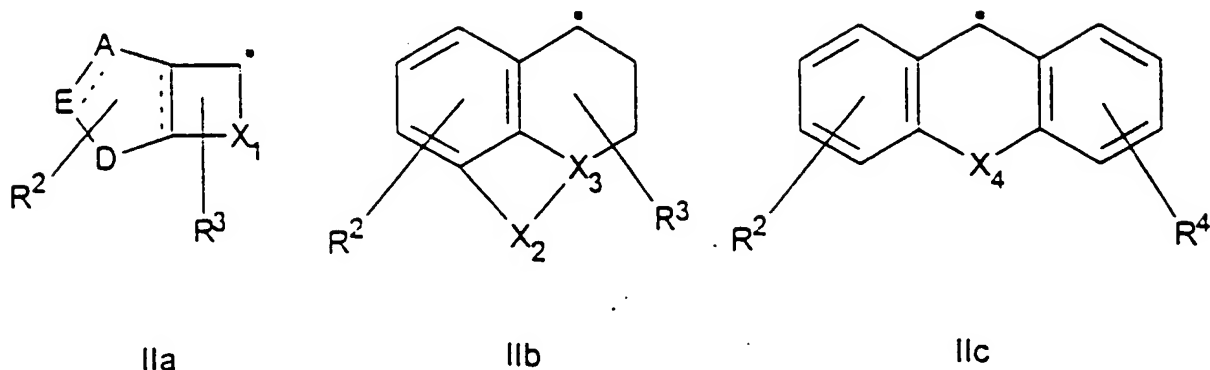
R<sup>18</sup> represents H, C<sub>1-4</sub> alkyl or CH<sub>2</sub>C(O)OR<sup>19</sup>;

R<sup>15</sup> and R<sup>17</sup> independently represent H, C<sub>1-6</sub> alkyl or C<sub>1-3</sub> alkylphenyl;

R<sup>1a</sup>, R<sup>1b</sup>, R<sup>1c</sup>, R<sup>11</sup> and R<sup>19</sup> independently represent H or C<sub>1-4</sub> alkyl; and

q represents 0, 1 or 2;

$R_x$  represents a structural fragment of formula IIa, IIb or IIc,



wherein

the dotted lines independently represent optional bonds;

A and E independently represent O or S, CH or CH<sub>2</sub> (as appropriate), or N or N(R<sup>21</sup>) (as appropriate);

D represents -CH<sub>2</sub>-, O, S, N(R<sup>22</sup>), -(CH<sub>2</sub>)<sub>2</sub>-, -CH=CH-, -CH<sub>2</sub>N(R<sup>22</sup>)-,  
 -N(R<sup>22</sup>)CH<sub>2</sub>-, -CH=N-, -N=CH-, -CH<sub>2</sub>O-, -OCH<sub>2</sub>-, -CH<sub>2</sub>S- or -SCH<sub>2</sub>-;

X<sub>1</sub> represents C<sub>2-4</sub> alkylene; C<sub>2-3</sub> alkylene interrupted by Z; -C(O)-Z-A<sup>1</sup> -;  
 -Z-C(O)-A<sup>1</sup> -; -CH<sub>2</sub>-C(O)-A<sup>1</sup> -; -Z-C(O)-Z-A<sup>2</sup> -; -CH<sub>2</sub>-Z-C(O)-A<sup>2</sup> -;  
 -Z-CH<sub>2</sub>-C(O)-A<sup>2</sup> -; -Z-CH<sub>2</sub>-S(O)<sub>m</sub>-A<sup>2</sup> -; -C(O)-A<sup>3</sup> -; -Z-A<sup>3</sup> -; or -A<sup>3</sup>-Z-;

X<sub>2</sub> represents C<sub>2-3</sub> alkylene, -C(O)-A<sup>4</sup> - or -A<sup>4</sup>-C(O)-;

X<sub>3</sub> represents CH or N;

X<sub>4</sub> represents a single bond, O, S, C(O), N(R<sup>23</sup>), -CH(R<sup>23</sup>)-,  
 -CH(R<sup>23</sup>)-CH(R<sup>24</sup>)- or -C(R<sup>23</sup>)=C(R<sup>24</sup>)-;

A<sup>1</sup> represents a single bond or C<sub>1-2</sub> alkylene;

$A^2$  represents a single bond or  $-CH_2-$ ;

$A^3$  represents  $C_{1-3}$  alkylene;

$A^4$  represents  $C(O)$  or  $C_{1-2}$  alkylene;

Z represents, at each occurrence, O,  $S(O)_m$  or  $N(R^{25})$ ;

$R^2$  and  $R^4$  independently represent one or more optional substituents selected from  $C_{1-4}$  alkyl,  $C_{1-4}$  alkoxy (which latter two groups are optionally substituted by one or more halo substituent), methylenedioxy, halo, hydroxy, cyano, nitro,  $S(O)_2NH_2$ ,  $C(O)OR^{26}$ ,  $SR^{26}$ ,  $S(O)R^{26a}$ ,  $S(O)_2R^{26a}$  or  $N(R^{27})R^{28}$ ;

$R^3$  represents one or more optional substituents selected from OH,  $C_{1-4}$  alkoxy,  $C_{1-6}$  alkyl (optionally substituted by one or more halo group), or  $N(R^{29a})R^{29b}$ ;

$R^{25}$ ,  $R^{29a}$  and  $R^{29b}$  independently represent H,  $C_{1-4}$  alkyl or  $C(O)R^{30}$ ;

$R^{26}$  represents H or  $C_{1-4}$  alkyl;

$R^{26a}$  represents  $C_{1-4}$  alkyl;

$R^{27}$  and  $R^{28}$  independently represent H,  $C_{1-4}$  alkyl or  $C(O)R^{30}$ , or together represent  $C_{3-6}$  alkylene, thus forming a 4- to 7-membered ring, which ring is optionally substituted, on a carbon atom that is  $\alpha$  to the nitrogen atom, with an  $=O$  group;

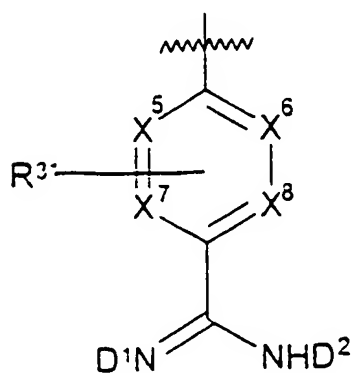
$R^{21}$ ,  $R^{22}$ ,  $R^{23}$ ,  $R^{24}$  and  $R^{30}$  independently represent, at each occurrence, H or  $C_{1-4}$  alkyl;

Y represents  $CH_2$ ,  $(CH_2)_2$ ,  $CH=CH$  (which latter group is optionally substituted by  $C_{1-4}$  alkyl),  $(CH_2)_3$ ,  $CH_2CH=CH$  or  $CH=CHCH_2$  (which latter three groups are optionally substituted by  $C_{1-4}$  alkyl, methylene,  $=O$  or hydroxy);

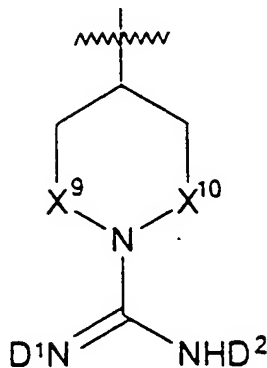
$R^y$  represents H or  $C_{1-4}$  alkyl;

n represents 0, 1, 2, 3 or 4; and

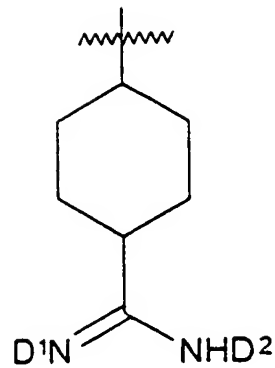
B represents a structural fragment of formula IIIa, IIIb or IIIc



IIIa



IIIb



IIIc

wherein

X<sup>5</sup>, X<sup>6</sup>, X<sup>7</sup> and X<sup>8</sup> independently represent CH, N or N-O;

X<sup>9</sup> and X<sup>10</sup> independently represent a single bond or CH<sub>2</sub>;

R<sup>31</sup> represents an optional substituent selected from halo, C<sub>1-4</sub> alkyl (which group is optionally substituted by one or more halo group), N(R<sup>32</sup>)R<sup>33</sup>, OR<sup>34</sup> or SR<sup>35</sup>;

R<sup>32</sup> and R<sup>33</sup> independently represent H, C<sub>1-4</sub> alkyl or C(O)R<sup>36</sup>;

R<sup>34</sup>, R<sup>35</sup> and R<sup>36</sup> independently represent H or C<sub>1-4</sub> alkyl; and

one of D<sup>1</sup> and D<sup>2</sup> represents H, and the other represents H, OR<sup>a</sup>, NHR<sup>a</sup>, C(=X<sup>11</sup>)X<sup>12</sup>R<sup>b</sup>, or D<sup>1</sup> and D<sup>2</sup> together represent a structural fragment of formula IVa:-

$R^a$  represents H or  $-A^5[X^{14}]_n[C(O)]_rR^e$ ;

$R^b$  represents  $-A^5[X^{14}]_n[C(O)]_rR^e$ ;

$A^5$  represents, at each occurrence, a single bond or  $C_{1-12}$  alkylene (which alkylene group is optionally interrupted by one or more O,  $S(O)_m$  and/or  $N(R^f)$  group, and is optionally substituted by one or more of halo, OH,  $N(H)C(O)R^g$ ,  $C(O)N(R^g)R^h$ ,  $C_{3-7}$ -cycloalkyl (which cycloalkyl group is optionally interrupted by one or more O,  $S(O)_m$  and/or  $N(R^f)$  group and/or is optionally substituted by one or more substituents selected from  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, halo, =O or =S), Het and  $C_{6-10}$  aryl (which aryl and Het groups are themselves optionally substituted by one or more substituents selected from  $C_{1-6}$  alkyl (optionally substituted by one or more halo substituent),  $C_{1-6}$  alkoxy, halo, cyano,  $C(O)OR^g$ ,  $C(O)N(R^g)R^h$  and  $N(R^f)R^g$ );

$R^c$  and  $R^d$  both represent H; or one of  $R^c$  and  $R^d$  represents H or  $C_{1-7}$  alkoxy and the other represents  $C_{1-17}$  alkyl (which alkyl group is optionally interrupted by one or more O atoms); or  $R^c$  and  $R^d$  together represent  $C_{3-8}$  cycloalkyl, which cycloalkyl group is interrupted by one or more O,  $S(O)_m$  and/or  $N(R^f)$  group;

$R^e$  represents, at each occurrence, H,  $C_{1-12}$  alkyl (which alkyl group is optionally interrupted by one or more O,  $S(O)_m$  and/or  $N(R^f)$  group, and/or is optionally substituted by one or more substituents selected from halo, OH,  $N(H)C(O)R^g$  and  $C(O)N(R^g)R^h$ ),  $A^7$ - $C_{3-7}$ -cycloalkyl (which cycloalkyl group is optionally interrupted by one or more O,  $S(O)_m$  and/or  $N(R^f)$  group and/or is substituted by one or more substituents selected from  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, halo, =O and =S),  $A^7$ - $C_{6-10}$  aryl or  $A^7$ -Het (which aryl and Het groups are optionally substituted by one or more substituents selected from  $C_{1-6}$  alkyl

(optionally substituted by one or more halo substituent), C<sub>1-6</sub> alkoxy, halo, cyano, C(O)OR<sup>g</sup>, C(O)N(R<sup>g</sup>)R<sup>h</sup> and N(R<sup>f</sup>)R<sup>g</sup>;

A<sup>7</sup> represents a single bond or C<sub>1-7</sub> alkylene (which alkylene group is optionally interrupted by one or more O, S(O)<sub>m</sub> and/or N(R<sup>f</sup>) group, and/or are optionally substituted by one or more of halo, OH, N(H)COR<sup>g</sup> and CON(R<sup>g</sup>)R<sup>h</sup>);

Het represents, at each occurrence, a five- to ten-membered heteroaryl group, which may be aromatic in character, containing one or more nitrogen, oxygen or sulphur atoms in the ring system;

n and r independently represent 0 or 1;

X<sup>11</sup>, X<sup>12</sup> and X<sup>14</sup> independently represent O or S;

X<sup>13</sup> represents O or N(R<sup>f</sup>);

R<sup>f</sup> represents, at each occurrence, H, C<sub>1-4</sub> alkyl or C(O)R<sup>g</sup>;

R<sub>g</sub> and R<sup>h</sup> independently represent, at each occurrence, H or C<sub>1-4</sub> alkyl; and

m represents, at each occurrence, 0, 1 or 2;

or a pharmaceutically acceptable salt thereof;

provided that:

(a) A and E do not both represent O or S;

(b) E and D do not both represent O or S;

(c) when R<sup>1</sup> represents OR<sup>1d</sup> and X<sub>1</sub> represents -C(O)-Z-A<sup>1</sup>,

-Z-CH<sub>2</sub>S(O)<sub>m</sub>-A<sup>2</sup>- or -Z-C(O)-Z-A<sup>2</sup>, then A<sup>1</sup> or A<sup>2</sup> (as appropriate) do not represent a single bond;

(f) when X<sub>4</sub> represents -CH(R<sup>23</sup>)-, R<sup>1</sup> does not represent OH;

(g) when A<sup>5</sup> represents a single bond, then n and r both represent 0;

- (f) when A<sup>5</sup> represents C<sub>1-12</sub> alkylene, then n represents 1;
- (g) when A<sup>5</sup> represents -CH<sub>2</sub>-, n is 1 and r is 0, then R<sup>e</sup> does not represent H; and
- (h) the compound is not:-
  - (S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Pro-Pab;
  - (R)- or (S)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Pro-Pab;
  - (S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;
  - (R)- or (S)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab;
  - 1-hydroxy-5-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;
  - 1-hydroxy-5,7-dimethyltetralin-1-yl-C(O)-Aze-Pab x HOAc;
  - 1-hydroxy-7-aminotetralin-1-yl-C(O)-Aze-Pab x HOAc;
  - 1-hydroxytetralin-1-yl-C(O)-Aze-Pab x HOAc;
  - 7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;
  - (R)- or (S)-7-methoxy-1-methyltetralin-1-yl-C(O)-Aze-Pab;
  - 4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab x OAc;
  - (S)- or (R)-1-hydroxy-4-methoxyindan-1-yl-C(O)-Aze-Pab;
  - 1-hydroxy-5-methoxytetralin-1-yl-C(O)-Aze-Pab(OH);
  - (S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(OH);
  - 4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab(OH);
  - 4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab(OMe);
  - (S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-
  - (C(O)OCH<sub>2</sub>CCl<sub>3</sub>);
  - (S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-
  - (C(O)OCH<sub>2</sub>CH<sub>3</sub>);

7-methoxy-1-allyltetralin-1-yl-C(O)-Aze-Pab x HOAc;  
(S)- or (R)-1-hydroxy-7-chlorotetralin-1-yl-C(O)-Pro-Pab;  
1-*n*-propyl-7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;  
6-chloro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
6,8-dichloro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
6-fluoro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
4-hydroxy-6-methylchroman-4-yl-C(O)-Aze-Pab x HOAc;  
8-chloro-4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab x HOAc;  
6-chloro-4-hydroxy-8-methylchroman-4-yl-C(O)-Aze-Pab x HOAc;  
(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-*i*-Pr);  
(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-Et);  
(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-Ch);  
(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-allyl);  
(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-Bzl);  
(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-  
(CO-O-methallyl);  
1-hydroxy-7-aminotetralin-1-yl-C(O)-Aze-Pab(OH);  
(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-Val);  
(S)- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-(Me)Pab; or  
9-hydroxyfluoren-9-yl-C(O)-Aze-Pab x HOAc.

2 (original). A compound as claimed in Claim 1 wherein R<sup>1</sup> represents OH or



C<sub>1-4</sub> alkyl (which latter group is optionally substituted by cyano or OH).

3 (currently amended). A compound as claimed in ~~any one of the preceding claims~~ claim 1 wherein R<sub>x</sub> represents a structural fragment of formula IIa or IIb.

4 (currently amended). A compound as claimed in ~~any one of the preceding claims~~ claim 1 wherein, when R<sub>x</sub> represents a structural fragment of formula IIa, then the dotted lines represent bonds, A and E both represent CH and D represents -CH=CH-;

5 (currently amended). A compound as claimed in ~~any one of the preceding claims~~ claim 1 wherein, when R<sub>x</sub> represents a structural fragment of formula IIa, X<sub>1</sub> represents optionally unsaturated C<sub>2</sub>- or C<sub>3</sub>-alkylene, or -Z-A<sup>3</sup> (in which Z represents O, S(O)<sub>m</sub> or N(R<sup>25</sup>) (in which R<sup>25</sup> is as defined in ~~Claim 1 above~~ or represents C<sub>1-4</sub> alkyl or C(O)R<sup>30</sup> and m and R<sup>30</sup> are as defined in ~~Claim 1 above~~) and A<sup>3</sup> represents C<sub>1</sub>- or C<sub>2</sub>-alkylene (which latter group is optionally unsaturated)).

6 (currently amended). A compound as claimed in ~~any one of the preceding claims~~ claim 1 wherein Y represents CH<sub>2</sub>, (CH<sub>2</sub>)<sub>2</sub> or (CH<sub>2</sub>)<sub>3</sub>.

7 (currently amended). A compound as claimed in ~~any one of the preceding claims~~ claim 1 wherein B represents a structural fragment of formula IIIa in which X<sup>5</sup>, X<sup>6</sup>, X<sup>7</sup> and X<sup>8</sup> all represent CH.

8 (currently amended). A compound as claimed in ~~any one of the preceding claims~~ claim 1 wherein, when D<sup>1</sup> and D<sup>2</sup> together represent a structural fragment of formula IVa, in which X<sup>13</sup> is O, then one of R<sup>c</sup> and R<sup>d</sup> represents H or C<sub>1-7</sub> alkoxy and the other represents C<sub>1-7</sub> alkyl.

9 (currently amended). A compound as claimed in ~~any one of Claims 1 to 7~~ claim 1, wherein, when D<sup>1</sup> or D<sup>2</sup> represents OR<sup>a</sup> and R<sup>a</sup> represents -A<sup>5</sup>[X<sup>14</sup>]<sub>n</sub>[C(O)]<sub>r</sub>R<sup>e</sup>, and

(i) A<sup>5</sup> is a single bond, then R<sup>e</sup> is:-

(1) A<sup>7</sup>-aryl, optionally substituted by one or more halo, C<sub>1-6</sub> alkoxy, C<sub>1-6</sub> alkyl or halo-C<sub>1-6</sub>-alkyl substituents; or

(2) H or linear, branched, optionally unsaturated, and/or cyclic, C<sub>1-12</sub> alkyl, which cyclic alkyl group is optionally interrupted by an O atom and, optionally, a further O atom or S(O)<sub>m</sub> group; or when

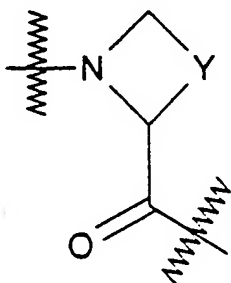
(ii) A<sup>5</sup> is linear or branched C<sub>1-12</sub> alkylene, X<sup>14</sup> is O and r is 0, then R<sup>e</sup> is C<sub>1-3</sub> alkyl or A<sup>7</sup>-aryl, in which A<sup>7</sup> is a single bond.

10 (currently amended). A compound as claimed in ~~any one of Claims 1 to 7 or 9~~ claim 1, wherein, when D<sup>1</sup> or D<sup>2</sup> represents OR<sup>a</sup>, then R<sup>a</sup> is H or C<sub>1-4</sub> alkyl.

11 (currently amended). A compound as claimed in ~~any one of Claims 1 to 7~~ claim 1, wherein, when D<sup>1</sup> or D<sup>2</sup> represents -C(=X<sup>11</sup>)X<sup>12</sup>R<sup>b</sup>, in which X<sup>11</sup> represents O

and  $X^{12}$  represents O or S, and, in which  $R^b$  group,  $A^5$  represents a single bond then  $R^9$  represents optionally unsaturated  $C_{1-6}$  alkyl,  $A^7$ - $C_{6-10}$ -aryl (in which  $A^7$  represents a single bond or  $C_{1-2}$  alkylene, and which  $A^7$ - $C_{6-10}$ -aryl group is optionally substituted by one or more halo,  $C_{1-4}$  alkyl and/or  $C_{1-4}$  alkoxy groups), or  $A^7$ - $C_{3-7}$ -cycloalkyl, in which  $A^7$  represents a single bond or linear or branched  $C_{1-7}$  alkylene, and which cycloalkyl group is optionally substituted by  $C_{1-3}$  alkyl.

12 (currently amended). A compound of formula I, as defined in ~~any one of the preceding claims~~claim 1, wherein the fragment



is in the S-configuration.

13 (currently amended). A pharmaceutical formulation including a compound as defined in ~~any one of Claims 1 to 12~~claim 1, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

14 (currently amended). A compound as defined in ~~any one of Claims 1 to 12~~claim 1, or a pharmaceutically acceptable salt thereof, for use as a pharmaceutical.

15 (currently amended). A compound as defined in ~~any one of Claims 1 to 12~~claim 1, or a pharmaceutically acceptable salt thereof, for use in the treatment of a condition where inhibition of thrombin is required.

16 (currently amended). A compound as defined in ~~any one of Claims 1 to 12~~claim 1, or a pharmaceutically acceptable salt thereof, for use in the treatment of thrombosis.

17 (currently amended). A compound as defined in ~~any one of Claims 1 to 12~~claim 1, or a pharmaceutically acceptable salt thereof, for use as an anticoagulant.

18 (currently amended). The use of a compound as defined in ~~any one of Claims 1 to 12~~claim 1, or a pharmaceutically acceptable salt thereof, as active ingredient in the manufacture of a medicament for the treatment of a condition where inhibition of thrombin is required.

19 (original). The use as claimed in Claim 18, wherein the condition is thrombosis.

20 (currently amended). The use of a compound as defined in ~~any one of Claims 1 to 12~~claim 1, or a pharmaceutically acceptable salt thereof, as active ingredient in the manufacture of an anticoagulant.

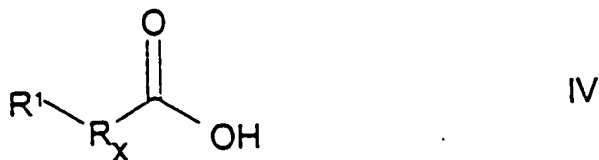
21 (currently amended). A method of treatment of a condition where inhibition of thrombin is required which method comprises administration of a therapeutically effective amount of a compound as defined in ~~any one of Claims 1 to 12~~claim 1, or a pharmaceutically acceptable salt thereof, to a person suffering from, or susceptible to, such a condition.

22 (original). A method as claimed in Claim 21, wherein the condition is thrombosis.

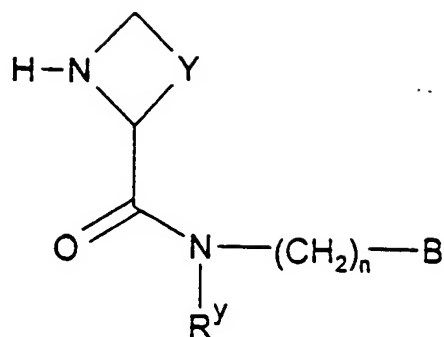
23 (original). A method as claimed in Claim 21, wherein the condition is hypercoagulability in blood and tissues.

24 (original). A process for the preparation of compounds of formula I which comprises:

- (i) the coupling of a compound of formula IV,

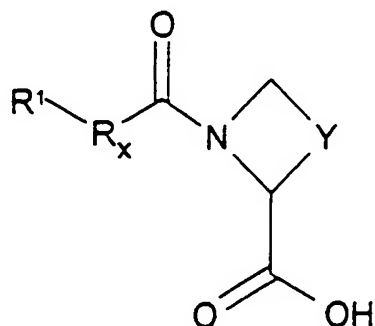


wherein  $\text{R}^1$  and  $\text{R}_x$  are as defined in Claim 1 with a compound of formula V,



wherein  $R^y$ , Y, n and B are as defined in Claim 1;

(ii) the coupling of a compound of formula VI,



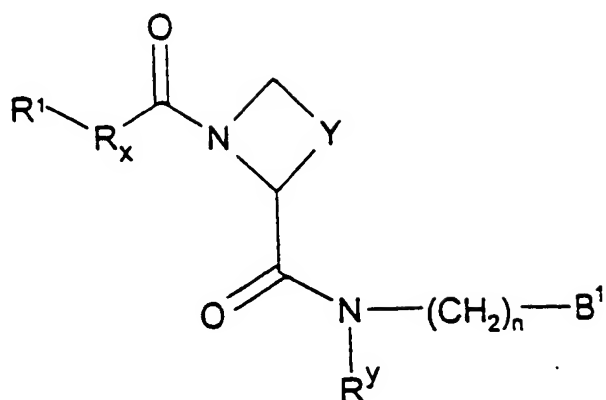
wherein  $R^1$ ,  $R_x$  and Y are as defined in Claim 1 with a compound of formula VII,



wherein  $R^y$ , n and B are as defined in Claim 1;

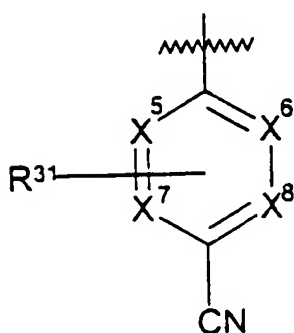
(iii) for compounds of formula I in which  $D^1$  or  $D^2$  represents  $OR^a$  or  $NHR^a$ ,

reaction of a compound of formula VIII,

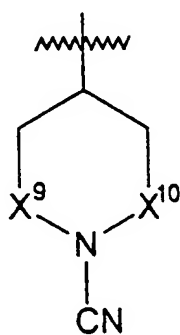


VIII

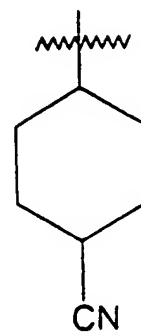
wherein B<sup>1</sup> represents a structural fragment of formula IIIId, IIIe or IIIf



IIIId



IIIe



IIIf

and R<sup>1</sup>, R<sub>x</sub>, Y, R<sup>y</sup>, n, R<sup>31</sup>, X<sup>5</sup>, X<sup>6</sup>, X<sup>7</sup>, X<sup>8</sup>, X<sup>9</sup> and X<sup>10</sup> are as defined in Claim 1 with  
 a compound of formula IX,



IX

wherein X<sup>a</sup> represents O or NH and R<sup>a</sup> is as defined in Claim 1;

(iv) for compounds of formula I in which D<sup>1</sup> or D<sup>2</sup> represents OR<sup>a</sup> or NHR<sup>a</sup>,  
 reaction of a compound of formula I in which D<sup>1</sup> or D<sup>2</sup> (as appropriate) represents

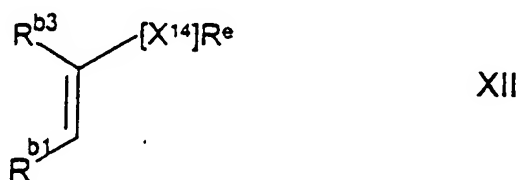
$C(O)OR^{b1}$ , in which  $R^{b1}$  represents a protecting group with a compound of formula IX as defined above;

(v) for compounds of formula I in which  $D^1$  or  $D^2$  represents  $OR^a$  or  $NHR^a$ ,  $R^a$  represents  $-A^5[X^{14}]_n[C(O)]_rR^e$ , in which  $A^5$  does not represent a single bond, and  $n$  represent 1, reaction of a compound of formula I in which  $D^1$  or  $D^2$  (as appropriate) represents  $OH$  or  $NH_2$ , with a compound of formula X,



wherein  $L^1$  represents a suitable leaving group,  $A^{5a}$  represents  $A^5$ , as defined in Claim 1 except that it does not represent a single bond, and  $X^{14}$ ,  $r$  and  $R^e$  are as defined in Claim 1;

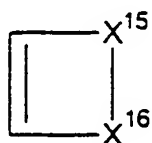
(vi) for compounds of formula I in which  $D^1$  or  $D^2$  represents  $OR^a$  or  $NHR^a$ ,  $R^a$  represents  $-A^5[X^{14}]_n[C(O)]_rR^e$ , in which  $A^5$  represents  $C_{2-12}$  alkylene, which alkylene group is branched at the carbon atom that is  $\alpha$  to the O or N atom of  $OR^a$  or  $NHR^a$  (as appropriate), and which group is optionally branched at the carbon atom that is  $\beta$  to that atom,  $n$  represents 1,  $r$  represents 0 and  $R^e$  is as defined in Claim 1, reaction of a compound of formula I in which  $D^1$  or  $D^2$  (as appropriate) represents  $OH$  or  $NH_2$ , with a compound of formula XI,





or a geometrical isomer thereof, or a mixture of such geometrical isomers, in which  $R^{b1}$  and  $R^{b3}$  each represent H or an alkyl group, provided that the total number of carbon atoms provided by  $R^{b1}$  and  $R^{b3}$  does not exceed 10, and wherein  $X^{14}$  and  $R^e$  are as defined in Claim 1;

(vii) for compounds of formula I in which  $D^1$  or  $D^2$  represents  $OR^a$  or  $NHR^a$ , represents  $-A^5[X^{24}]_n[C(O)]_rR^e$ , in which  $A^5$  represents a single bond, and  $R^e$  represents  $A^7$ -C<sub>3-6</sub>-cycloalkyl, in which  $A^7$  represents a single bond, and the cycloalkyl group is interrupted by at least one O or S atom, which atom is between the carbon atom at the point of attachment to the O or NH group of  $OR^a$  or  $NHR^a$ , and a carbon atom that is  $\alpha$  to that point of attachment, and which cycloalkyl group is optionally interrupted by one or more O or S(O)<sub>m</sub> group and/or optionally substituted by one or more =O group, reaction of a compound of formula I, in which  $D^1$  or  $D^2$  (as appropriate) represents OH or NH<sub>2</sub>, with a compound of formula XII,



XII

wherein  $X^{15}$  represents O or S and  $X^{16}$  represents C<sub>1-4</sub> alkylene (which alkylene group is optionally interrupted by one or more O or S(O)<sub>m</sub> group and/or optionally substituted by one or more =O group);

(viii) for compounds of formula I in which D<sup>1</sup> or D<sup>2</sup> represents C(X<sup>11</sup>)X<sup>12</sup>R<sup>b</sup>, reaction of a compound of formula I in which D<sup>1</sup> and D<sup>2</sup> both represent H with a compound of formula XIII,



wherein L<sup>2</sup> represents a suitable leaving group, and X<sup>11</sup>, X<sup>12</sup> and R<sup>b</sup> are as defined in Claim 1;

(ix) for compounds of formula I in which D<sup>1</sup> and D<sup>2</sup> together represent a structural fragment of formula IVa, reaction of a corresponding compound of formula I in which D<sup>1</sup> or D<sup>2</sup> represents OH or NHR<sup>f</sup> (in which R<sup>f</sup> is as defined in Claim 1), with a compound of formula XV,



wherein R<sup>c1</sup> and R<sup>c2</sup> both represent -OR<sup>c3</sup>, in which R<sup>c3</sup> represents C<sub>1-3</sub> alkyl, or together represent =O, and R<sup>c</sup> and R<sup>d</sup> are as defined in Claim 1;

(x) for compounds of formula I in which one or more of X<sup>5</sup>, X<sup>6</sup>, X<sup>7</sup> and X<sup>8</sup> represent N-O, oxidation of a corresponding compound of formula I in which X<sup>5</sup>, X<sup>6</sup>, X<sup>7</sup> and/or X<sup>8</sup> (as appropriate) represent(s) N; or

(xi) for compounds of formula I in which any one of Z, X<sub>1</sub>, R<sup>2</sup>, R<sup>4</sup>, A<sup>5</sup>, A<sup>7</sup>, R<sup>c</sup>, R<sup>d</sup> and/or R<sup>e</sup> comprises or includes a (O) or a S(O)<sub>2</sub> group, oxidation of a corresponding compound of formula I (or a compound corresponding to a compound of formula I) wherein Z, X<sub>1</sub>, R<sup>2</sup>, R<sup>4</sup>, A<sup>5</sup>, A<sup>7</sup>, R<sup>c</sup>, R<sup>d</sup> and/or R<sup>e</sup> (as appropriate) comprise(s) or include(s) a S group;

(xii) for compounds of formula I in which D<sup>1</sup> and D<sup>2</sup> both represent H, removal of a OR<sup>a</sup>, NHR<sup>a</sup> or C(=X<sup>11</sup>)X<sup>12</sup>R<sup>b</sup> group (in which R<sup>a</sup>, R<sup>b</sup>, X<sup>11</sup> and X<sup>12</sup> are as defined in

Claim 1), or removal of a structural fragment of formula IVa as defined in Claim 1, from a corresponding compound of formula I; or

(xiii) introduction and/or interconversion of a substituent on an aromatic and/or non-aromatic, carbocyclic and/or heterocyclic ring in a corresponding compound of formula I.